

CONCLUSIONS. In a patient with severe and repeated attacks of asthma the pulmonary distention continued for several weeks after a cessation of a prolonged attack. This distention caused the heart to assume a vertical position, but did not influence its surface area. During the attack of asthma the diaphragm moved but slightly, and movements in reverse of the normal were observed. In explaining such reversed movements, however, one must take into account the excessive thoracic movements which act on the diaphragmatic attachments. The movements of these attachments may more than neutralize the movements due to the diaphragmatic contractions, so that the crests of the diaphragm may seem to execute reversed movements.

A CONTRIBUTION TO THE STUDY OF HEREDITARY DEGENERATION (PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY IN COMBINATION WITH DEGENERATION IN THE CENTRAL NERVOUS SYSTEM).

By CARL D. CAMP, M.D.,

CLINICAL PROFESSOR OF DISEASES OF THE NERVOUS SYSTEM IN THE MEDICAL DEPARTMENT OF THE UNIVERSITY OF MICHIGAN, ANN ARBOR, MICHIGAN.

WHEN only certain parts of the nervous system are congenitally defective they are likely to be those having close functional relations to each other, and in consequence there develop in such cases certain functional disturbances which enable the nature and location of the anatomic lesion to be diagnosticated with accuracy. It is well known also that these defects may not be apparent until the individual has attained a certain age, when, seemingly from the mere stress of living, the defective parts undergo retrogressive changes, and symptoms of disability appear, the nature of which depends upon the functions of the part affected. In these cases of so-called abiotrophy a strong reason for believing that the anatomic change and the resulting clinical phenomena are congenital in origin is their tendency to become a characteristic of certain families.

The literature of these family degenerative conditions is quite extensive, but for the most part the published studies on the subject may be divided into those which deal with the localization and character of the histopathologic changes in the nervous system or other tissues involved and those concerned with attempts to classify them into types according to the symptoms presented or the parts affected, which are then considered as separate and

distinct diseases. A study of the literature leads to the conclusion that there are in all these cases histopathologic changes of a degenerative character in the various tissues, and that the clinical types depend largely, if not solely, on the location of the lesion. From this it follows that if there was present in the parental organism a toxic substance or disease capable of causing degenerative changes in the nervous system or elsewhere, and this toxic substance or disease could be transmitted to offspring, those offspring might show similar degenerative changes. Under such circumstances we would be dealing not with an hereditary degeneration but with a degeneration due to disease or toxemia possibly preventable or treatable. The question arises whether we have any way of differentiating a truly hereditary characteristic from an acquired degenerative condition caused by a neurotoxin transmitted from parent to child.

These dystrophies, when they affect the nervous system, give rise to various fairly definite symptom-complexes, such as Friedreich's ataxia, family spastic paraplegia, etc. The muscular dystrophies are also divided into various types: the pseudohypertrophic form of Duchenne; the juvenile form described by Erb; Leyden's form; the facioscapulohumeral type (Landouzy-Dejerine); Zimmerlin type, beginning in the thorax muscles and affecting the upper extremities before the lower; a type described by Jendrassik as congenital, that is, the manifestations begin at birth; and the Werdnig-Hoffman type, beginning in infancy and affecting several members of the same family, but so frequently these types are combined with each other or present anomalous characteristics that we have the authority of Erb¹ that their differentiation is a matter of great difficulty. They are usually familial, and are regarded as quite distinct from the spinal type of progressive muscular atrophy; and from the neural, or Charcot-Marie-Tooth type, variations of which are described by Gombault, Dejerine-Scottas, Eichorst, Brossard, and others. It is certain, however, that progressive spinal muscular atrophy may be hereditary, as in the case reported by A. Strümpell² and in a similar case reported by Bernhardt.³ If such is the fact we have an instance of a condition usually regarded as due to some unknown, acquired cause becoming hereditary. There are two possible explanations: one is that an acquired degeneration has become hereditary, which is opposed to Weismann's theory of heredity; or that the cause of the degeneration in the parent was transmitted to the offspring and became in turn the cause of the degeneration there. The observations of William G. Spiller⁴ that syphilis might be a cause

¹ Deutsch. med. Woch., 1910, S. 1865.

² Deutsch. Zeitschr. f. Nervenheilk., 1893, Band iii, S. 471.

³ Virchow's Archiv, Band cxv, Heft 2, S. 197.

⁴ Jour. Nerv. and Ment. Dis., 1912, p. 584.

of the so-called primary lateral sclerosis and of progressive spinal muscular atrophy, and the case recorded by S. Leopold² of progressive spinal muscular atrophy, in which necropsy showed some evidence of syphilis, suggests at least one such cause that can be acquired and can also be transmitted to the offspring.

As bearing on this question, I wish to record a case observed by me in which a parent and probably also a grandparent had the spinal type of progressive muscular atrophy, while the patient presented the classical picture of the pseudohypertrophic form of muscular dystrophy. The occurrence of such a case indicates a close relationship between these two conditions.

John C., aged three years, was admitted to the Hospital of the University of Michigan November 20, 1909. His mother was well. His father could not be examined, but, according to the description furnished, was suffering from a disability which began with wasting of the small muscles of both hands, producing a clawhand, and this wasting had extended up both arms to the shoulders. The affection was painless and not accompanied by any change in the sensibility of the hands, and there was no involvement of the lower extremities. It may be inferred that he was suffering from the progressive muscular atrophy of the spinal type. Chronic anterior poliomyelitis may be ruled out by the statement that the atrophy was quite pronounced before any marked weakness was noticed. There was also a statement that the patient's grandfather on the father's side had an affection similar to the father's, but an accurate description of his condition was unobtainable. The mother of the patient had had one miscarriage before he was born, and the patient had a younger brother apparently well.

The patient was born at full term, with instruments, and was seemingly normal and uninjured. He learned to talk at the age of ten months and to walk at one year. He had measles in the summer before his admission to the hospital, and a light attack of pneumonia at the same time. His present trouble apparently began when he was about the age of two years, when some difficulty in walking was noticed, and this became progressively worse until his admission to the hospital. An examination at that time showed a child of about normal size for his age, hair light and fine, a well-nourished appearance, intelligent expression, and a well-shaped head. He understood and obeyed commands, answered questions readily, and appeared to have a normal mentality. The pupils were equal, reacted to light and in accommodation, and there were no extraocular palsies. The ocular fundi appeared normal. There was no paralysis of the face or tongue. The arms, forearms, and shoulders were rather thin, but all movements were normal, and there was no fibrillary tremor. There was no atrophy of the small

² Jour. Nerv. and Ment. Dis., 1912, p. 606.

muscles of the hands. When standing there was a marked lumbar lordosis and protrusion of the abdomen; this was present also when sitting or lying on his side; it disappeared when lying on his back. There was no lateral curvature of the spine. The thighs appeared to be about the normal size, but the calves of both legs were distinctly larger than normal, and felt very firm. There was no paralysis or deformity of the legs or feet and he could walk without support, but has a waddling, typically dystrophic gait. In arising from a prone position he turned over and rose on his hands and knees. He then attempted to rise to a standing position by pushing with his arms, but was apparently too weak to do so without assistance. The biceps-jerks were present on both sides, but the knee-jerks and Achilles-jerks were not obtained. No sensory loss could be detected anywhere. The skin reflexes were all present. Plantar irritation caused flexion of the toes.

While the age of the patient suggests the Werdnig-Hoffman type of muscular dystrophy, a pseudohypertrophy such as was present here rules out that diagnosis according to Hoffman.⁶ We have then an instance of progressive spinal muscular atrophy in the father and grandfather and pseudohypertrophic muscular dystrophy in the child. I have not been able to find a similar case of heredity in the literature, but K. Mendel⁷ reported a case in which the symptoms of progressive spinal muscular atrophy were combined with those of a pseudohypertrophic muscular dystrophy in a boy, aged sixteen years. The condition was not hereditary.

Eulenberg and Cohn,⁸ under the title of "family dystrophic heredodegeneration," reported four members of the same family, aged from eight to sixteen years, affected with a progressive muscular atrophy beginning in the face and upper extremities and accompanied by pseudohypertrophy of the calves and lost knee-jerks, but they regarded these cases as a peculiar type of muscular dystrophy rather than as a combination of types.

While the dystrophies are usually hereditary, and thereby differ from the progressive spinal muscular atrophies which are not, usually, there are many cases of muscular dystrophy in which no hereditary influence can be detected. I have seen a boy, aged twelve years, suffering from a typical muscular dystrophy of the pseudohypertrophic type, but the most careful inquiries failed to show any trace of hereditary degeneration. The parents were healthy and not blood relations. They had two other children, one older and one younger than the patient, who were normal. All of the grandparents and the aunts and uncles of the patient were living, and showed no apparent abnormality. The patient

⁶ Deut. Zeitschr. f. Nervenheilk., 1893, S. 427; *ibid.*, 1897, S. 292; *ibid.*, 1898, S. 418.

⁷ Neurolog. Centralbl., 1901, S. 601.

⁸ *Ibid.*, 1911, S. 963.

presented typical signs and symptoms of the disease, which it would be unnecessary to record in detail.

It is not uncommon to find atypical cases of muscular dystrophy or combinations of two or more types in the same patient, as Erb has pointed out. It is, however, much less common to find the combination of a muscular dystrophy with the spinal heredo-degenerations. Such cases do occur, however, and are of considerable clinical importance, primarily because of the liability to errors in diagnosis.

The following case is an instance of the combination of Friedreich's ataxia with a pseudohypertrophic muscular dystrophy in the same patient:

Carl K., aged ten years, was admitted to the Hospital of the University of Michigan July 24, 1912. On his admission the following history was obtained from his parents:

His father and mother were living and well, and the patient had two sisters, one five years old and one seven, both in good health. There were no nervous disorders on the father's side of the family but the mother said that she had two brothers; the older one was well, but the younger one had an affection similar to the patient's, coming on at the age of ten and causing his death at the age of eighteen years. Her father and his brothers were free of any nervous disorder, but her mother's brother had a similar complaint, beginning at ten and fatal at eighteen years.

The patient was a first child, and was delivered with instruments, but apparently not hurt. He was bottle-fed, and had diarrhea in his first year. He walked and talked at about the usual age, and appeared to be a normal child. Measles and whooping cough were the only infectious diseases he had, and there was no history of injury. He had never had any convulsions.

At an early age, about four years, it was noticed that he had some difficulty in walking—a waddling gait—and this difficulty slowly increased; but about one year before his admission to the hospital his gait became much worse, and it was noticed that he walked on his toes. About June 1, 1912, he became unable to walk at all. He had severe headaches for about a year, usually coming two or three times a week, and his father stated that his school work was poor for this year; he seemed to have difficulty in learning, and also was forgetful. He had no other symptoms.

On examination, July 26, 1912, it was noted that he seemed to be a well-nourished, intelligent boy, with few stigmas of deviation and no stigmas of hereditary syphilis.

The pupils were equal, and reacted to light and in accommodation. There was a distinct nystagmus on lateral deviation of the eyeballs. There was no paralysis or atrophy of the face or tongue. There was no disturbance in speech or deglutition. The grip of both hands was weak, especially the left. He could raise both

arms above his head, but his power to resist passive movement of the elbows and shoulders was less than normal. There was no atrophy or deformity of the hands, arms, or shoulders, no fibrillary tremor and no ataxia in the finger to nose test, with the eyes open or closed. The biceps-jerks and triceps-jerks were not obtained on either side. The patient sat in his wheel chair leaning forward on his elbows. He could not walk and could stand only if all his weight was supported from his shoulders. He stood on his toes. The thighs and buttocks were normally developed for his age, but the calves of both legs were abnormally large and felt firm on pres-

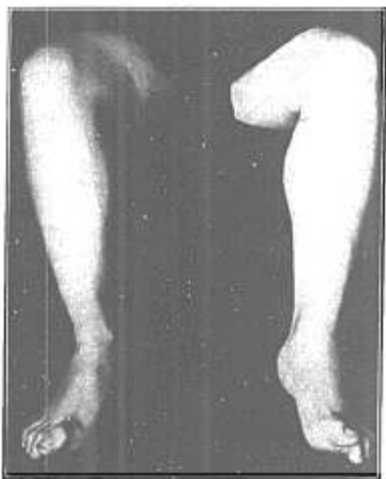


FIG. 1.—Pseudohypertrophic muscular dystrophy and Friedreich's ataxia, showing the 'Friedreich foot.' The foot is shortened, and there is permanent hyperextension of the proximal phalanx and flexion of the terminal phalanx of the great toe. Note also the pseudohypertrophy of the calf muscles.

sure. There was a distinct talipes equinus in both feet, with hyperextension of the first phalangeal joint of the great toes and flexion of the terminal joint (Fig. 1). There was no atrophy of the small muscles of the feet. All normal movements of the legs and feet were possible but weak. The knee-jerks were present on both sides, but were diminished. The Achilles-jerks were present on both sides. Plantar irritation caused extension of the great toe on each side. The cremasteric and abdominal reflexes were present on both sides. Tactile sensation was normal on the face, body, and extremities, and the localization of sensation was normal on

the legs and feet. There was no analgesia or thermaesthesia, and no loss of the sense of motion or position in the fingers or toes. A general physical examination was negative. The urine examination showed a specific gravity of 1020; no albumin; no glucose; no bile; urea, normal amount; sediment was normal. An examination in the ophthalmologic clinic, by Dr. Walter Parker, showed: nystagmus on lateral deviation of the eyeball; pupils equal; reflexes normal; no gross lesion.

July 29. Began taking x-ray treatments to the spine three times a week. A "soft tube" was used and the distance about 12 inches. Ten minutes exposure was given the entire spine.

July 31. Blood count showed: red blood cells, 4,500,000; leukocytes, 10,000; hemoglobin, 85 per cent.

He was re-examined in August and September, with practically the same findings. The headaches entirely disappeared after the first week of x-ray treatments, and he was able to stand by grasping a small topped table and resting his chest against it. In standing this way his back was bent forward and his legs widely separated; if the buttocks were supported he showed a marked lumbar lordosis. Irritation of the soles of the feet produced extension of the toes on each side and also a movement of withdrawal of the entire leg ("reaction of defence," Babinski). A general physical examination showed nothing pathologic in the viscera, no glandular enlargement, and a normal development of the external genitalia. A Wassermann reaction on the blood was negative, and examination of the cerebrospinal fluid showed no abnormal chemical or cellular constituents.

Cases of Friedreich's ataxia and muscular dystrophy have been reported by Jendrassik,⁹ with an anatomic study by Kollaritis.¹⁰ Cases are also reported by Baumlín¹¹ and Bing.¹² A similar case but without any family history of either disease is reported by Jastrowitz.¹³ Cases of muscular dystrophy, such as the one reported by O. Crouzon,¹⁴ in which there was present a positive Babinski sign, and that of H. Schlesinger,¹⁵ in which the patient developed a pes equino valgus in both feet early in the disease, are cases somewhat resembling these. Greenfield¹⁶ reported a case of Friedreich's disease combined with the peroneal type of progressive muscular atrophy. Cases of spastic spinal paralysis, nystagmus, and tremor are reported Jendrassik,¹⁷ who refers to similar cases

⁹ Deutsch. Zeitschr. f. Nervenheilk., 1902, S. 444.

¹⁰ Deutsch. Archiv f. klin. Med., 1901, Band lxx, S. 157.

¹¹ Deutsch. Zeitschr. f. Nervenheilk., 1901, S. 265.

¹² Deutsch. Archiv. f. klin. Med., 1905, S. 109.

¹³ Neurolog. Centralbl., 1911, S. 426.

¹⁴ Revue Neurologique, 1912, p. 109.

¹⁵ Neurolog. Centralbl., 1901, S. 143.

¹⁶ Proc. Royal Soc. Med., London, v, No. 3, Neurol. Sec., p. 75.

¹⁷ Deutsch. Archiv. f. klin. Med., 1897, Band lviii, S. 137.

reported by Maas, Seeligmüller, and Hoffman. These cases probably represent still another combination of hereditodegenerative conditions.

A case of pseudohypertrophic muscular dystrophy combined with optic neuritis is not mentioned by Jendrassik¹⁸ in his collection of transitional and combination types of hereditodegenerations. Such a case was admitted to my service at the Hospital of the University of Michigan May 27, 1912:

Floyd B., aged eight years, complained chiefly of difficulty in walking. No history of the case was obtainable except from the patient himself, who said that his mother was dead and that his father had deserted the family. He said that he had three brothers, and they all had trouble similar to his. He did not remember that he ever had any serious illness, but said that he never went to school and that he could not read or write. An examination on his admission to the hospital showed a pleasant, well-mannered child, who obeyed all simple commands, dressed and undressed himself, untied knots normally, and was about the average size for a child of nine years. His head was of normal shape, his ears rather prominent, and Darwin tubercles were present on both ears. The pupils were equal, reacted to light and in accommodation. The extraocular movements were normal. There was no facial palsy. The tongue protruded straight, and there was no tremor or atrophy of the tongue. The masseters and temporals contracted well and equally. He had no difficulty in moving his head. There was no tremor of the hands on extension. There was no disturbance of the gross movements of the arms, and there was no incoordination of the hands in the finger to nose test. The muscular strength in the arms in flexion and extension was equal and good in both arms. There was no atrophy or deformity of the arms or hands and no fibrillary tremors were noticed. The grip was equal and good in both hands. The patient walked with a broad base, but there was no ataxia and no apparent spasticity in the legs. His station was equally as good with his eyes open as with them closed. There was marked weakness in extension of the legs and dorsoflexion of the feet equal on both sides. The muscular strength in flexion of the legs was fair. Both extension and flexion of the thighs were weak, although the patient could flex and extend the thighs if no resistance was offered. On standing erect there was a forward curvature of the lumbar spine and bulging of the abdomen. He appeared to elevate the hips in walking. The musculature of the calves of the legs appeared large and bulging (Fig. 2). No unusual development in the musculature of the thighs was present, and there was apparently no atrophy of the thigh muscles. He felt pinpoint equally well over both sides

¹⁸ Lewandowsky's *Handbuch der Neurologie*, Berlin, 1911, Band ii, S. 397.

of the face. There was no anesthesia of the conjunctivæ. He felt pinpoint and light touch over both sides of the back, both sides of the abdomen, and both sides of the thorax. Pinpoint was felt equally well over both lower extremities all over. There was no disturbance of sensation of any form over the arms. The elbow-jerks and knee-jerks were not obtained. The Achilles-jerks were equal and about normal. The conjunctival reflex was present. The umbilical reflex and the cremasteric reflexes were present. Plantar irritation caused plantar flexion of the toes on both sides. He was well-nourished, and an examination of the heart, lungs, and abdominal viscera showed nothing abnormal. The examination of the blood and urine was negative. The blood pressure was 115 mm. Hg. A Wassermann reaction on the blood was reported negative.



FIG. 2.—Pseudohypertrophic muscular dystrophy and optic neuritis.

May 31. Patient was examined by Dr. Walter Parker, who found: Tension O. U., normal. Pupillary reflexes active, normal to direct and consensual light and in accommodation.

Ophthalmoscopic examination: O. D., media clear. Disk margins completely blurred, slightly hyperemic, swollen between 1 and 2 diopters. The temporal side of the disk at the area of the muscular bundle apparently was not swollen. There were some irregular grayish-white changes near the nasal border of the disk, with one or two spots of pigment; these changes were like irregular, inconspicuous branched lines. There was a peculiar stippling of the whole fundus quite marked between the macula and the disk. The veins pulsated. O. S., the disk was swollen, particularly on the nasal side, and there was an oblique position of the disk, the obliquity being so great that the disk seemed to face toward the macula, and the temporal side of the disk was nearly obscured. This was undoubtedly due to an oblique position of the scleral foramen, the optic nerve entering obliquely. The apparent amount of swelling was 3 diopters.

Choroid: There was an area of choroidal change near the nasal border of the disk nearly a disk diameter in size. In this area there was some pigment displacement and a short, crescent-shaped

streak, lighter in color at the outer border of the pigmented area, nearly parallel to the disk border. At the nasal border of the disk there was a small, grayish, rounded area about one-half disk diameter in width, over which the retinal vessels could be distinctly seen. The whole choroid was stippled with grayish pigmentation. There were no pigmentary changes in the periphery of the fundus.

Diagnosis: O. D., optic neuritis. O. S., same as O. D., with localized choroiditis. Two months later the condition was unchanged.

The diagnosis of pseudohypertrophic muscular dystrophy can be made in this case with certainty, but most interesting is the presence, in association with this condition, of a bilateral optic neuritis of a peculiar type. That this is an example of hereditary optic neuritis seems most likely, for the reason that all the details of the ophthalmoscopic findings correspond closely to those described by Hormuth¹⁹ as present in such cases. Furthermore, there was a family history of some similar affection and an absence of any symptoms or signs of intracranial disease to cause optic neuritis and no history or sign of any poisoning.

While the most obvious interest in the cases above recorded lies in questions of diagnosis, they are perhaps more valuable for the evidence they furnish as to the etiology of such conditions. In the cases of dystrophy ordinarily seen there is a tendency to the transmission of the same type of defect from parent to offspring usually a fairly definite type, and the defect apparently is transmitted as are other family traits. If all cases were of that kind there would be little objection to the view that "heredity" was a sufficient etiology, even though we would still be in the dark as to the primary causal factor. When we find a case in which one type in a parent is followed by another type of degeneration in the offspring, or when, as in the last two cases, we find degenerative changes variously localized, it seems more probable that something truly external is acting on the organism, attacking the weaker parts. Generally, true heredity acts in a way which is distinctly opposed to degeneration. According to Lugaro,²⁰ "Degeneration is a disturbance of physiologic hereditary transmission it is a disease of the hereditary mechanism." The cause of degeneration is something external acting on the organism, and this factor may vary in successive generations. Degeneration therefore is a result of disease of the stock, but a disease that may be curable. If that is true, and the evidence furnished by the above cases seems to confirm such a view, it is of great importance that it be generally recognized.

¹⁹ Beitrag zur Lehre von den Hereditären Schnervenleiden, Hamburg, 1900.

²⁰ Trans. by Orr and Rows, Modern Problems in Psychiatry, Manchester, 1909.